

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (original) An oxygen-resistant iron hydrogenase derived from an oxygen sensitive iron hydrogenase by the substitution of one or more amino acid residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase.
- 2-26. (cancelled)
27. (new) The oxygen-resistant iron hydrogenase of claim 1, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with a synthetic and/or derivatized amino acid having properties that limit O₂ diffusion through the channel while allowing H₂ diffusion out of the channel.
28. (new) The oxygen-resistant iron hydrogenase of claim 1, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with tryptophan, isoleucine, leucine, or phenylalanine.
29. (new) The oxygen-resistant iron hydrogenase of claim 1, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with bulky and/or hydrophobic residues.
30. (new) The oxygen-resistant iron hydrogenase of claim 29, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with at least one bulky residue that projects close to a catalytic site having a bimetallic center containing two iron atoms.
31. (new) The oxygen-resistant iron hydrogenase of claim 29, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with at least one bulky residue that partially shields an Fe₂-atom.
32. (new) The oxygen-resistant iron hydrogenase of claim 29, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with leucine and/or isoleucine that projects into the hydrogen channel.
33. (new) The oxygen-resistant iron hydrogenase of claim 29, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted

with at least one hydrophobic residue and wherein the hydrophobic residue adds bulk to the hydrophobic surface of the channel.

34. (new) The oxygen-resistant iron hydrogenase of claim 29, wherein the one or more residues within the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with at least one bulky residue that narrows the channel opening at a protein surface-solvent boundary.

35. (new) An oxygen-resistant iron hydrogenase comprising an hydrogen channel having a diameter defined by one or more diameter determining amino acid residues, wherein the diffusion of oxygen within the channel is reduced as compared to the diffusion of oxygen in the hydrogen channel of an oxygen-sensitive iron hydrogenase.

36. (new) The oxygen-resistant iron hydrogenase of claim 35, wherein one or more residues that line the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently replaced with bulky and/or hydrophobic residues.

37. (new) The oxygen-resistant iron hydrogenase of claim 35, wherein one or more residues that line the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently replaced with tryptophan, isoleucine, leucine, or phenylalanine.

38. (new) The oxygen-resistant iron hydrogenase of claim 35, wherein one or more residues that line the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently replaced with a synthetic and/or derivatized amino acid having properties that limit O₂ diffusion through the channel while allowing H₂ diffusion out of the channel.

39. (new) The oxygen-resistant iron hydrogenase of claim 35, wherein one or more residues that line the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently replaced with a residue that has a side chain volume larger than the side chain volumes of the amino acid at the same position in the oxygen-sensitive iron hydrogenase.

40. (new) An oxygen-resistant iron hydrogenase comprising a derivative of an oxygen-sensitive iron hydrogenase, wherein one or more amino acid residues within an hydrogen channel in the oxygen-resistant hydrogenase are substituted to reduce the oxygen sensitivity of the oxygen-resistant iron hydrogenase.

41. (new) The oxygen-resistant iron hydrogenase of claim 40, wherein the average channel size is between about 5.0 and about 2.4 Å in diameter.

42. (new) The oxygen-resistant iron hydrogenase of claim 40, wherein the average channel size is between about 3.5 and about 2.4 Å in diameter.
43. (new) The oxygen-resistant iron hydrogenase of claim 40, wherein one or more residues that line the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with bulky and/or hydrophobic residues.
44. (new) The oxygen-resistant iron hydrogenase of claim 40, wherein one or more residues that line the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with tryptophan, isoleucine, leucine, or phenylalanine.
45. (new) The oxygen-resistant iron hydrogenase of claim 40, wherein one or more residues that line the hydrogen channel of the oxygen-sensitive iron hydrogenase are independently substituted with a synthetic and/or derivatized amino acid having properties that limit O₂ diffusion through the channel while allowing H₂ diffusion out of the channel.